Image 1743 AFF

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/340165
Filing Date	June 28, 1999
First Named Inventor	NOVAK
Art Unit	1743
Examiner Name	Alexander
Attorney Docket Number	SBCCOM

Total Number of Pages in This Submission: 101

ENCLOSURES *(Check all that apply)*

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance communication to Group
- [X] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please Identify below):

Appeal Brief (3) copies

Remarks: 33 pages each brief

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	US Army Material Command
Signature	William Randolph
Date	Jan 29, 2004

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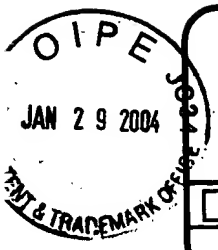

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 330

Complete if Known	
Application Number	09/340165
Filing Date	June 28, 1999
First Named Inventor	NOVAK
Examiner Name	Alexander
Art Unit	1743
Attorney Docket No.	SBCcom

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 19-2201

Deposit Account Name:

The Director is authorized to: *(check all that apply)*

☒ Charge fee(s) indicated below ☒ Credit any overpayments

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below		Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	330
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 330

SUBMITTED BY				(Complete *(if applicable)*)	
Name *(Print/Type)*	William Randolph	Registration No. *(Attorney/Agent)*	28986	Telephone	703 806-8254
Signature	William Randolph			Date	Jan 29, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: NOVAK, Thaddeus J. Examiner: ALEXANDER, Lyle

Serial Number: 09/340,165 Group Art Unit: 1743

Filing Date: June 28, 1999

Title: MICROSPOT TEST KIT AND METHOD FOR CHEMICAL TESTING

APPEAL BRIEF

FILED UNDER 37 C.F.R. 1.192

Honorable Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

This appeal is being filed in response to the Final Rejection dated August 29, 2003 of claims 13-27, as set forth in Appendix A. The following is being provided as required in 37 C.F.R. 1.192(c):

1. Real Party In Interest: The real party in interest is the Army Materiel Command, U.S. Department of the Army, U.S. Government.

2. Related Appeals And Interferences: There are no related appeals or interferences that have been filed.

3. Status Of Claims: Claims 1 through 11 and 13 through 27 are pending in the application. Claims 1 – 11 have been allowed. Claims 13 – 27 have been rejected.

4. Status Of Amendments: No amendments have been filed subsequent to the Final Rejection of August 29, 2003.

5. Summary Of The Invention:

This is a Continuation-In-Part of U.S. Application Serial No. 08/763,181, filed December 11, 1996, now U.S. Patent No. 5,935,862.

The micro spot test system and methodology of the present invention relates to an apparatus and method for the testing of analytes contained in a sample by dissolving the analytes in a selected solvent and utilizing capillary deposition techniques to concentrate the analytes on sorbent materials. Detector reagents are pre-deposited on the sorbent materials to form different reaction sites or regions for receiving the analyte solution. Detection sensitivity and accuracy for a range of concentrations of analytes is provided by depositing the analyte solution by capillary action to different regions of particular sorbent materials containing the selected detector reagents so that the analytes become concentrated at the particular spot or point of deposition on the sorbent material. The analyte solutions are deposited by placing small diameter tubes containing the analyte solution in contact with the surface of the sorbent material so that the solutions are drawn from the tubes by capillary action. The detector reagents, sorbent materials, and solvent

are selected so that the analytes are concentrated at the spot where the small diameter tube contacts the sorbent layer.

A system for chromogenically detecting the presence of chemical analytes includes a means for obtaining a sample solution containing the analytes; a device for the capillary deposition of the sample solution; chromatographic sorbent materials; and chromogenic detector reagents which have been pre-deposited on the sorbent materials. Storage devices may be provided for the samples and for the sample solutions, capillary deposition devices, and the chromatographic sorbent materials containing the pre-deposited chromogenic detector reagents.

The micro spot system and methodology of detecting the presence of target analytes in a sample comprises the application of a solution containing the analytes to a chromatographic sorbent material by capillary action. Sufficient amounts of chromogenic detector reagents to form chromogenic indicators when a target analyte is present in the sample have been pre-deposited on the chromatographic sorbent material at different sites to receive the solution containing the analytes. Apparatus for accomplishing this is generally shown in Figures 1 - 5. In Figures 1 - 5, the apparatus or kit 11 includes a bag or container 12 for storing the components of the system; at least one thin layer chromatographic plate (TLC) plate 13; collecting devices such as cloth wipes 18 or swabs 19 for wiping surfaces for chemical residues; solvent containers 22; containers 23 for receiving the swabs and solvent solutions; and small diameter capillary or microcapillary tubes 25.. Solvents for the samples are stored in separate bottles 22. The plate 13 is provided with score lines 14 to divide the plate 13 into a plurality of individual test sites 15. A different reagent has been pre-deposited on each test site 15, as

generally depicted by regions 16 in Figure 1. To ensure long shelf-life stability of the reagents that have been deposited on the sorbent material, the plate 13 could be packaged in a plastic bag which contains an inert gas or which has been vacuum- sealed in an inert atmosphere. Additionally, the plates 13 and test sites 15 can be marked or coded to identify a particular type of test, such as water quality, where the different reagent sites 16 are also identified.

For purposes of this application, the term sample is defined as a representative fraction of the material that is to be processed and tested to detect the presence of an analyte. The sample may be a solid, such as soil, a liquid, such as water taken from a lake, or a vapor, such as fumes obtained from a chemical plant. An analyte is a chemical substance present in the samples that are being tested or analyzed. A solution is a homogeneous liquid that contains dissolved chemical substances. A sample solution is a homogeneous liquid that contains dissolved chemical substances (i.e., the analytes or solutes) and which is derived by washing, extracting, or eluting a sample with a solvent or mixture of solvents. A sample solution is obtained for analysis by washing, extracting or eluting the wipe in a container 23 with a suitable solvent such as acetone, dichloromethane, hexane, etc. Soil samples can be washed, extracted or eluted in separate containers to obtain sample solutions. Aqueous samples suspected of containing a target analyte can be extracted with an immiscible solvent which is capable of extracting the analytes believed to be therein. In addition, solid phase extraction (SPE) or solid phase microextraction (SPME) techniques can be used to extract analytes from water for analysis using the micro spot tests. (see page 6, line 14 to page 7, line 9).

Once the solution or liquid extract has been formed, and where necessary the extract has been concentrated by evaporation, a tube with a small diameter bore or opening 36, such as a small diameter capillary or microcapillary tube is used to collect and dispense small amounts of the solution onto the surface of plate 13 by capillary action. The plates 13 can be thin layer chromatographic plates or TLC plates having a surface layer formed of a chromatographic sorbent material. (see page 9, lines 9 – 17 and page 14, line 9 to page 17, lne 15 of the specification).

The term "microcapillary tube" includes any tube made from glass, plastic or other material having a small diameter opening that is capable of dispensing liquid from (or drawing liquid into) the opening by capillary action. (see page 10, line 8 to page 12, line 2 of the specification).

The micro spot test method is generally solvent dependent, with respect to both the solvents for the analyte and the detector reagent. In general, the solvent for target analytes should be selected so that the analytes are concentrated in a small spot when the solution containing the analytes is applied to a sorbent plate with a microcapillary tube.

The micro spot test is conducted by first applying the detector reagent to the TLC plate and allowing the solvent for the detector reagent to evaporate. Then, the solution containing the analyte is applied to the sorbent media or TLC plate. For this procedure, a detector reagent should be selected that is insoluble (or has very low solubility) in the solvent that is used to dissolve the analyte. If the detector reagent has some solubility in the solvent for the analyte, in a positive test result, a ring of the indicator may form instead of a small spot. Consequently, the detection sensitivity for the analyte may be poorer. Attractive advantages of applying the detector reagent to a TLC plate prior to

applying the solutions containing the analyte(s) include (a) the liquid detector reagent solutions do not need to be prepared just prior to the test, (b) the required detector reagents can be pre-deposited at different locations on the same TLC media prior to on-site testing, and (c) the actual on-site testing steps are reduced to the microcapillary deposition of solutions containing the analytes and visual observation of the results.

6. Issues For Appeal:

a. Whether claims 13-16 are unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak, et. al. (U.S. Patent No. 4,346,001).

b. Whether claims 17-27 are unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001).

7. Grouping Of The Claims (for each ground of rejection):

a. Rejection of claims 13-16 for being unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak et. al. (U.S. Patent 4,346,001). The claims of the group do not stand and fall together and have been further grouped since they present different patentable features.

(1) Claims 13 and 16. Claim 13 recites a system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising a means for obtaining a solution containing the analyte; tube means for receiving the solution containing the analyte, where the tube means has an end portion with a microcapillary sized opening formed therein for dispensing the analyte solution by capillary action; sorbent material means having a detector reagent pre-deposited in the sorbent material for

detecting the presence of the analyte, the sorbent material means receiving the analyte solution from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the analyte solution is deposited on the sorbent material means by capillary action. The detector reagent has been pre-deposited in the sorbent material and the analyte is adsorbed by and concentrated in the sorbent material and remains at the spot of contact between the end portion of the tube means with the sorbent material means. Dependent claim 16 recites a further feature of the invention of claim 13, where the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

(2) Claim 14. Dependent claim 14 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening.

(3) Claim 15. Dependent claim 15 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means.

b. Rejection of claims 17-27 for being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001). The claims of the group do not stand and fall together and have been further grouped since they present different patentable features.

(1) Claim17. Dependant claim 17 recites a further feature of the system of claim 13 where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters.

(2) Claim 18. Dependent claim 18 recites a further feature of the system of claim 13 where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters.

(3) Claim 19. Dependent claim 19 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer.

(4) Claim 20. Dependent claim 20 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent.

(5) Claim 21. Dependent claim 21 recites a further feature of the system of claim 20 where the detector reagent is selected from the group consisting of bromcresol green;

7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

(6) Claim 22. Dependent claim 22 recites a further feature of the system of claim 13 where the the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

(7) Claim 23. Dependent claim 23 recites a further feature of the system of claim 13 where the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane,

petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(8) Claim 24. Dependent claim 24 recites a further feature of the system of claim 13 where the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(9) Claim 25. Dependent claim 25 recites a further feature of the system of claim 13 where the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution

with a pH in the range 2-12, dimethylsulfoxide, N-methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(10) Claim 26. Dependent claim 26 recites a further feature of the method of claim 2 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

(11) Claim 27. Dependent claim 27 recites a further feature of the system of claim 13 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

8. Arguments

a. Rejection of claims 13 through 16 as being unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak et. al. (U.S. Patent 4,346,001). The claims of the group have been grouped above in paragraph 7.

(1) Claims 13 and 16. Claim 13 recites a system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising a means for obtaining a solution containing the analyte; tube means for receiving the solution containing the analyte, where the tube means has an end portion with a microcapillary sized opening formed therein for dispensing the analyte solution by capillary action; sorbent material means having a detector reagent pre-deposited in the sorbent material for detecting the presence of the analyte, the sorbent material means receiving the analyte

solution from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the analyte solution is deposited on the sorbent material means by capillary action. Tyihak does not appear to teach a sorbent material means having a detector reagent pre-deposited in the sorbent material and the sorbent material means adsorbing and concentrating the analyte at the spot of contact between the end portion of the tube means with the sorbent material means. Further, Tyihak does not suggest that the analyte remains at the spot of contact.

Dependent claim 16 recites a further feature of the invention of claim 13, where the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

This is a continuation-in-part of U.S. Patent Application Serial No. 08/763,181, filed December 11, 1996 and issued August 10, 1999 as U.S. Patent No. 5,935,862. In the prosecution of U.S. Patent No. 5,935,862, it was pointed out **to the present examiner** that the present invention is not determining the presence of analytes, such as chemical warfare agents, by thin layer chromatography (TLC) techniques where movement/migration of the analyte occurs on the thin layer chromatography TLC plate as discussed in Tyihak. A plate coated with a thin layer of sorbent chromatographic material that has been marketed for use in performing thin layer chromatographic (TLC) experiments where the unknown/analyte is identified by the migration patterns in the TLC plate. In direct contrast to Tyihak and general TLC procedures, the invention set forth in the subject patent application sets forth a method and system where for accurate chromatographic identification, the analyte remains concentrated at the spot of deposition

of the analyte solution by capillary action onto the sorbent material. By selective use of particular combinations of sorbent materials, solvents and detector reagents, the analyte remains concentrated at the spot of deposition and the results of the tests are highly discernible. The present invention collects the analyte in a small spot on a solid support, such as a sorbent plate, by applying a solution of the analyte to the solid support by capillary deposition using tubes with microcapillary sized openings of from about 0.05 to about 1.6 millimeters. The analyte is then detected by chromogenic detector reagents that have been predeposited in the sorbent material.

When performing TLC experiments, the analyte is eluted with an eluant (i.e., a solvent or mixtures of solvents), which results in the sample migrating and separating into distinct spots, where the number of spots depends upon the number of components in the sample. Since diffusion occurs as the components migrate up the TLC plate, the spots obtained after elution of the analyte mixture are less concentrated than when the analyte was originally spotted on the TLC plate. Therefore, the method of the present invention is not thin layer chromatography (TLC), and can best be described as the opposite of TLC or a non-TLC procedure. This distinction is discussed, for example, in pages 2 and 3 of the present patent application. In TLC, the components of the analytes separate, but with the present invention components of the analyte do not separate but are concentrated at a small spot where they are deposited on the plate by capillary action. Migration of the analyte on the TLC plate is contrary to optimization of the results of the present invention. As a result, better detection sensitivity is obtained from the present invention when compared to TLC and other spot test methods. TLC methods reported in the literature often cite lower levels of detection of analytes at the 100, 50, 10 and 1

microgram levels. In the present invention, detection of analytes at the 100 nanogram (0.1 microgram) and 10 nanogram levels occur, as discussed on page 30 of the specification. The specification sets forth that the test method of the present invention is generally solvent dependent, with respect to the solvents for the analyte and the detector reagent, and the polarity of the sorbent material.

As understood, Tyihak discloses a linear overpressurized thin-layer chromatographic apparatus where capillary tubes 6 and 7 are connected to a sorbent layer plate 1. The samples are fed into the apparatus containing the sorbent layer by overpressure applied to the capillary tube, column 4, lines 49-55. Further, the analyte does not appear to remain at the place of deposition, but migrates across the sorbent plate under pressure.

It is further believed that the invention disclosed in this application is sufficiently distinct from TLC, even though a common feature is the use of sorbent plates. Even waiving this argument still leaves a core result that the present invention is able to detect chromatographic sensitivities much greater than those obtained with conventional TLC methods. Further the microspot test and system of the present invention does not utilize an elution step, and the analyte compounds are not generally separated when the microspot test method is performed

For the reasons cited above, Tyihak does not appear to disclose, teach or show a sorbent material means having a detector reagent pre-deposited in the sorbent material and the sorbent material means adsorbing and concentrating the analyte at the spot of contact between the end portion of the tube means with the sorbent material means.

Further, Tyihak does not suggest that the analyte remains at the spot or place of contact between the end portion of the tube means with the sorbent material.

(2) Claim 14. Dependent claim 14 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening. Tyhak, as understood, does not appear to disclose or teach the limitation where the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening (see page 11, line 15 to page 12, line 2 of the specification).

(3) Claim 15. Dependent claim 15 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means. Tyhak, as understood, does not appear to disclose or teach the limitation where the thickness of the end wall is at least twice the diameter of the microcapillary sized opening, (see page 11, line 15 to page 12, line 2 of the specification)

b. Rejection of claims 17-27 for being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001). The claims of the group do

not stand and fall together and have been further grouped since they present different patentable features.

(1) Claim17. Dependant claim 17 recites a further feature of the system of claim 13 where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters. Tyhak, as understood, does not appear to either disclose or teach the limitation where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters, (see page 9, lines 20 to 22 of the specification).

(2) Claim 18. Dependent claim 18 recites a further feature of the system of claim 13 where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters. Tiyhak, as understood, does not appear to either disclose or teach the limitation where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters, (see page 9, line 18 to page 10, line 5 of the specification).

(3) Claim 19. Dependent claim 19 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer. As understood, Tihyak does not appear to suggest or teach a sorbent material comprising a thin layer chromatographic sheet provided with a silica gel surface layer.

(4) Claim 20. Dependent claim 20 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent. As understood, Tihyak does not appear to suggest or teach a sorbent material comprising a thin layer chromatographic sheet provided with a polysilic acid sorbent.

(5) Claim 21. Dependent claim 21 recites a further feature of the system of claim 20 where the detector reagent is selected from the group consisting of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine. As understood, Tihyak does not appear to suggest or teach a detector reagent selected from the above identified group and pre-deposited in the sorbent material.

(6) Claim 22. Dependent claim 22 recites a further feature of the system of claim 13 where the the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material. As understood, Tihyak does not appear to suggest or teach a sorbent material formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

(7) Claim 23. Dependent claim 23 recites a further feature of the system of claim 13 where the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of sorbent materials and solvents.

(8) Claim 24. Dependent claim 24 recites a further feature of the system of claim 13 where the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected

from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of solvents and sorbent materials.

(9) Claim 25. Dependent claim 25 recites a further feature of the system of claim 13 where the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution with a pH in the range 2-12, dimethylsulfoxide, N-methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-

butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of solvents and sorbent materials.

(10) Claim 26. Dependent claim 26 recites a further feature of the method of claim 2 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination. **The rejection of this claim is not understood since it depends from an allowed claim 2, see copy of allowed claims in Appendix B.**

(11) Claim 27. Dependent claim 27 recites a further feature of the system of claim 13 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector

reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination. As understood, Tihyak does not appear to suggest or teach the selected sorbent materials.

It is requested that the rejections of all pending claims be reversed and all pending claims be allowed.

January 29, 2004

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9. **Appendix A: Appealed Claims**

Claims 13 through 27, as amended, are Appealed

13. (Twice Amended) A system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising:

means for obtaining a solution containing the analyte;

tube means for receiving the solution containing the analyte, the tube means having an end portion with a microcapillary sized opening formed therein for dispensing the solution containing the analyte by capillary action;

sorbent material means having a detector reagent pre-deposited in the sorbent material for detecting the presence of the analyte, the sorbent material means receiving the solution containing the analyte from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the solution containing the analyte is deposited on the sorbent material means by capillary action where the detector reagent has been pre-deposited and with the analyte being adsorbed by and concentrated in the sorbent material and remaining at the spot of contact between the end portion of the tube means with the sorbent material means for combining with the detector reagent.

14. The system according to claim 13, wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening.

15. (Once Amended) The system according to claim 13, wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means.

16. The system according to claim 13, wherein the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

17. The system according to claim 13, wherein the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters.

18. The system according to claim 13, wherein the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters.

19. (Once Amended) The system according to claim 13, wherein the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer.

20. (Once Amended) The system according to claim 13, wherein the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent.

21. The system according to claim 20, wherein the detector reagent is selected from the group consisting of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

22. The system according to claim 13, wherein the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

23. The system according to claim 13, wherein the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the

solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

24. The system according to claim 13, wherein the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

25. The system according to claim 13, wherein the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution with a pH in the range 2-12, dimethylsulfoxide, N-

methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

26. The method of claim 2, wherein the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

27. The system according to claim 13, wherein the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top

layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

10. **Appendix B: Allowed Claims**

Claims 1 through 11, as amended, have been **allowed.**

1.(Once Amended) A method of detecting the presence of an analyte, comprising the steps of:

placing a chromogenic or fluorogenic detector reagent for detecting the presence of the analyte on a chromatographic sheet or medium containing sorbent material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, and mixtures of therof;

placing the analyte in a solution where the solvent for the analyte consists of a non-aqueous solvent selected from the group of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane;

placing the solution containing the analyte in a tube having an end portion with a microcapillary sized opening, so that when the tube is placed in contact with a chromatographic sheet having a surface layer formed of sorbent material, the solution containing the analyte is withdrawn from the end portion of the tube and onto the surface layer of the sorbent material by capillary action;

placing the end portion of the tube having the microcapillary sized opening in contact with the sorbent material at the place where the detector reagent has been deposited on the sorbent material so that the solution containing the analyte is withdrawn from the tube by capillary action, the solvent being absorbed into the sorbent material and the analyte being separated from the solvent, and wherein the analyte remains at the spot of application and wherein the analyte is analyzed at this spot of application.

2. (Once Amended) A method of screening a solution for an analyte that has been dissolved in a solvent to form the solution and for detecting the presence of the analyte when the solution is deposited in a sorbent material so that the analyte is separated from the solvent at the place of application to the sorbent material, comprising the steps of:

placing a detector reagent for detecting the presence of the analyte on the sorbent material;

placing the solution containing the analyte in a tube having an end portion forming a microcapillary sized opening in the end portion of the tube so that when the tube is placed in contact with the sorbent material, the solution containing the analyte in the tube is withdrawn from the end portion of the tube and into the sorbent material by capillary action;

placing the end portion of the tube forming the microcapillary sized opening in contact with the sorbent material at the location where the detector reagent is placed on the sorbent material, so that the solution is withdrawn from the tube by capillary action, the solvent being absorbed into the sorbent material and the analyte being separated from the solvent and adsorbed by the sorbent material at the spot of application, wherein the analyte remains at the spot of application and is analyzed at this same spot.

3. The method of claim 2, wherein the diameter of the microcapillary sized opening has range of diameters of from about 0.05 to about 1.6 millimeters.

4. The method of claim 2, wherein the sorbent material is formed of a polar material selected from the group consisting of silica gel, high performance thin layer

chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is less polar than the sorbent material and selected from the group of ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

5. The method of claim 2, wherein the sorbent material comprises a thin layer chromatographic medium containing a silica gel or polysilicic acid sorbent and the solvent for the analyte is selected from the group consisting of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexane, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

6. The method of claim 2, wherein the detector reagent is selected from the group of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenylacetate, sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-

dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M); ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodide plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

7. The method of claim 6, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide, and the solvent for the analyte is selected from solvents that are less polar than the sorbent material and selected from the group consisting of ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

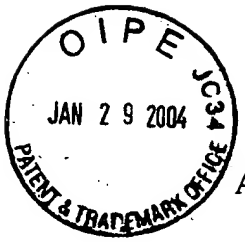
8. The method of claim 2, wherein the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and mixtures thereof, and the solvent for the analyte is selected from the group consisting of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

9. The method of claim 2, wherein sorbent material is formed of a polar chromatographic material and the solvent for the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

10. The method of claim 2, wherein the sorbent material is formed of a non-polar material selected from the group of reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, and the solvent for the analyte is an aqueous solvent mixture containing solvents selected from the from the group of water, methanol, acetonitrile, and acetone.

11. The method of claim 2, wherein the sorbent material is formed of an ion-exchange material selected from the group of anion exchange resin, cation exchange resin and diethylaminoethylcellulose and the solvent for the analyte comprises water.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicant: NOVAK, Thaddeus J. Examiner: ALEXANDER, Lyle

Serial Number: 09/340,165 Group Art Unit: 1743

Filing Date: June 28, 1999

Title: MICROSPOT TEST KIT AND METHOD FOR CHEMICAL TESTING

APPEAL BRIEF

FILED UNDER 37 C.F.R. 1.192

Honorable Commissioner of Patents and Trademarks

Washington, D.C. 20231

Sir:

This appeal is being filed in response to the Final Rejection dated August 29, 2003 of claims 13-27, as set forth in Appendix A. The following is being provided as required in 37 C.F.R. 1.192(c):

1. Real Party In Interest: The real party in interest is the Army Materiel Command, U.S. Department of the Army, U.S. Government.

2. Related Appeals And Interferences: There are no related appeals or interferences that have been filed.

3. Status Of Claims: Claims 1 through 11 and 13 through 27 are pending in the application. Claims 1 – 11 have been allowed. Claims 13 – 27 have been rejected.

4. Status Of Amendments: No amendments have been filed subsequent to the Final Rejection of August 29, 2003.

5. Summary Of The Invention:

This is a Continuation-In-Part of U.S. Application Serial No. 08/763,181, filed December 11, 1996, now U.S. Patent No. 5,935,862.

The micro spot test system and methodology of the present invention relates to an apparatus and method for the testing of analytes contained in a sample by dissolving the analytes in a selected solvent and utilizing capillary deposition techniques to concentrate the analytes on sorbent materials. Detector reagents are pre-deposited on the sorbent materials to form different reaction sites or regions for receiving the analyte solution. Detection sensitivity and accuracy for a range of concentrations of analytes is provided by depositing the analyte solution by capillary action to different regions of particular sorbent materials containing the selected detector reagents so that the analytes become concentrated at the particular spot or point of deposition on the sorbent material. The analyte solutions are deposited by placing small diameter tubes containing the analyte solution in contact with the surface of the sorbent material so that the solutions are drawn from the tubes by capillary action. The detector reagents, sorbent materials, and solvent

are selected so that the analytes are concentrated at the spot where the small diameter tube contacts the sorbent layer.

A system for chromogenically detecting the presence of chemical analytes includes a means for obtaining a sample solution containing the analytes; a device for the capillary deposition of the sample solution; chromatographic sorbent materials; and chromogenic detector reagents which have been pre-deposited on the sorbent materials. Storage devices may be provided for the samples and for the sample solutions, capillary deposition devices, and the chromatographic sorbent materials containing the pre-deposited chromogenic detector reagents.

The micro spot system and methodology of detecting the presence of target analytes in a sample comprises the application of a solution containing the analytes to a chromatographic sorbent material by capillary action. Sufficient amounts of chromogenic detector reagents to form chromogenic indicators when a target analyte is present in the sample have been pre-deposited on the chromatographic sorbent material at different sites to receive the solution containing the analytes. Apparatus for accomplishing this is generally shown in Figures 1 - 5. In Figures 1 - 5, the apparatus or kit 11 includes a bag or container 12 for storing the components of the system; at least one thin layer chromatographic plate (TLC) plate 13; collecting devices such as cloth wipes 18 or swabs 19 for wiping surfaces for chemical residues; solvent containers 22; containers 23 for receiving the swabs and solvent solutions; and small diameter capillary or microcapillary tubes 25.. Solvents for the samples are stored in separate bottles 22. The plate 13 is provided with score lines 14 to divide the plate 13 into a plurality of individual test sites 15. A different reagent has been pre-deposited on each test site 15, as

generally depicted by regions 16 in Figure 1. To ensure long shelf-life stability of the reagents that have been deposited on the sorbent material, the plate 13 could be packaged in a plastic bag which contains an inert gas or which has been vacuum- sealed in an inert atmosphere. Additionally, the plates 13 and test sites 15 can be marked or coded to identify a particular type of test, such as water quality, where the different reagent sites 16 are also identified.

For purposes of this application, the term sample is defined as a representative fraction of the material that is to be processed and tested to detect the presence of an analyte. The sample may be a solid, such as soil, a liquid, such as water taken from a lake, or a vapor, such as fumes obtained from a chemical plant. An analyte is a chemical substance present in the samples that are being tested or analyzed. A solution is a homogeneous liquid that contains dissolved chemical substances. A sample solution is a homogeneous liquid that contains dissolved chemical substances (i.e., the analytes or solutes) and which is derived by washing, extracting, or eluting a sample with a solvent or mixture of solvents. A sample solution is obtained for analysis by washing, extracting or eluting the wipe in a container 23 with a suitable solvent such as acetone, dichloromethane, hexane, etc. Soil samples can be washed, extracted or eluted in separate containers to obtain sample solutions. Aqueous samples suspected of containing a target analyte can be extracted with an immiscible solvent which is capable of extracting the analytes believed to be therein. In addition, solid phase extraction (SPE) or solid phase microextraction (SPME) techniques can be used to extract analytes from water for analysis using the micro spot tests. (see page 6, line 14 to page 7, line 9).

Once the solution or liquid extract has been formed, and where necessary the extract has been concentrated by evaporation, a tube with a small diameter bore or opening 36, such as a small diameter capillary or microcapillary tube is used to collect and dispense small amounts of the solution onto the surface of plate 13 by capillary action. The plates 13 can be thin layer chromatographic plates or TLC plates having a surface layer formed of a chromatographic sorbent material. (see page 9, lines 9 – 17 and page 14, line 9 to page 17, lne 15 of the specification).

The term "microcapillary tube" includes any tube made from glass, plastic or other material having a small diameter opening that is capable of dispensing liquid from (or drawing liquid into) the opening by capillary action. (see page 10, line 8 to page 12, line 2 of the specification).

The micro spot test method is generally solvent dependent, with respect to both the solvents for the analyte and the detector reagent. In general, the solvent for target analytes should be selected so that the analytes are concentrated in a small spot when the solution containing the analytes is applied to a sorbent plate with a microcapillary tube.

The micro spot test is conducted by first applying the detector reagent to the TLC plate and allowing the solvent for the detector reagent to evaporate. Then, the solution containing the analyte is applied to the sorbent media or TLC plate. For this procedure, a detector reagent should be selected that is insoluble (or has very low solubility) in the solvent that is used to dissolve the analyte. If the detector reagent has some solubility in the solvent for the analyte, in a positive test result, a ring of the indicator may form instead of a small spot. Consequently, the detection sensitivity for the analyte may be poorer. Attractive advantages of applying the detector reagent to a TLC plate prior to

applying the solutions containing the analyte(s) include (a) the liquid detector reagent solutions do not need to be prepared just prior to the test, (b) the required detector reagents can be pre-deposited at different locations on the same TLC media prior to on-site testing, and (c) the actual on-site testing steps are reduced to the microcapillary deposition of solutions containing the analytes and visual observation of the results.

6. Issues For Appeal:

a. Whether claims 13-16 are unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak, et. al. (U.S. Patent No. 4,346,001).

b. Whether claims 17-27 are unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001).

7. Grouping Of The Claims (for each ground of rejection):

a. Rejection of claims 13-16 for being unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak et. al. (U.S. Patent 4,346,001). The claims of the group do not stand and fall together and have been further grouped since they present different patentable features.

(1) Claims 13 and 16. Claim 13 recites a system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising a means for obtaining a solution containing the analyte; tube means for receiving the solution containing the analyte, where the tube means has an end portion with a microcapillary sized opening formed therein for dispensing the analyte solution by capillary action; sorbent material means having a detector reagent pre-deposited in the sorbent material for

detecting the presence of the analyte, the sorbent material means receiving the analyte solution from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the analyte solution is deposited on the sorbent material means by capillary action. The detector reagent has been pre-deposited in the sorbent material and the analyte is adsorbed by and concentrated in the sorbent material and remains at the spot of contact between the end portion of the tube means with the sorbent material means. Dependent claim 16 recites a further feature of the invention of claim 13, where the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

(2) Claim 14. Dependent claim 14 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening.

(3) Claim 15. Dependent claim 15 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means.

b. Rejection of claims 17-27 for being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001). The claims of the group do not stand and fall together and have been further grouped since they present different patentable features.

(1) Claim17. Dependant claim 17 recites a further feature of the system of claim 13 where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters.

(2) Claim 18. Dependent claim 18 recites a further feature of the system of claim 13 where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters.

(3) Claim 19. Dependent claim 19 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer.

(4) Claim 20. Dependent claim 20 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent.

(5) Claim 21. Dependent claim 21 recites a further feature of the system of claim 20 where the detector reagent is selected from the group consisting of bromcresol green;

7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

(6) Claim 22. Dependent claim 22 recites a further feature of the system of claim 13 where the the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

(7) Claim 23. Dependent claim 23 recites a further feature of the system of claim 13 where the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane,

petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(8) Claim 24. Dependent claim 24 recites a further feature of the system of claim 13 where the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(9) Claim 25. Dependent claim 25 recites a further feature of the system of claim 13 where the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution

with a pH in the range 2-12, dimethylsulfoxide, N-methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

(10) Claim 26. Dependent claim 26 recites a further feature of the method of claim 2 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

(11) Claim 27. Dependent claim 27 recites a further feature of the system of claim 13 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

8. Arguments

a. Rejection of claims 13 through 16 as being unpatentable under 35 U.S.C. 102(b) as being clearly anticipated by Tyihak et. al. (U.S. Patent 4,346,001). The claims of the group have been grouped above in paragraph 7.

(1) Claims 13 and 16. Claim 13 recites a system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising a means for obtaining a solution containing the analyte; tube means for receiving the solution containing the analyte, where the tube means has an end portion with a microcapillary sized opening formed therein for dispensing the analyte solution by capillary action; sorbent material means having a detector reagent pre-deposited in the sorbent material for detecting the presence of the analyte, the sorbent material means receiving the analyte

solution from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the analyte solution is deposited on the sorbent material means by capillary action. Tyihak does not appear to teach a sorbent material means having a detector reagent pre-deposited in the sorbent material and the sorbent material means adsorbing and concentrating the analyte at the spot of contact between the end portion of the tube means with the sorbent material means. Further, Tyihak does not suggest that the analyte remains at the spot of contact.

Dependent claim 16 recites a further feature of the invention of claim 13, where the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

This is a continuation-in-part of U.S. Patent Application Serial No. 08/763,181, filed December 11, 1996 and issued August 10, 1999 as U.S. Patent No. 5,935,862. In the prosecution of U.S. Patent No. 5,935,862, it was pointed out **to the present examiner** that the present invention is not determining the presence of analytes, such as chemical warfare agents, by thin layer chromatography (TLC) techniques where movement/migration of the analyte occurs on the thin layer chromatography TLC plate as discussed in Tyihak. A plate coated with a thin layer of sorbent chromatographic material that has been marketed for use in performing thin layer chromatographic (TLC) experiments where the unknown/analyte is identified by the migration patterns in the TLC plate. In direct contrast to Tyihak and general TLC procedures, the invention set forth in the subject patent application sets forth a method and system where for accurate chromatographic identification, the analyte remains concentrated at the spot of deposition

of the analyte solution by capillary action onto the sorbent material. By selective use of particular combinations of sorbent materials, solvents and detector reagents, the analyte remains concentrated at the spot of deposition and the results of the tests are highly discernible. The present invention collects the analyte in a small spot on a solid support, such as a sorbent plate, by applying a solution of the analyte to the solid support by capillary deposition using tubes with microcapillary sized openings of from about 0.05 to about 1.6 millimeters. The analyte is then detected by chromogenic detector reagents that have been predeposited in the sorbent material.

When performing TLC experiments, the analyte is eluted with an eluant (i.e., a solvent or mixtures of solvents), which results in the sample migrating and separating into distinct spots, where the number of spots depends upon the number of components in the sample. Since diffusion occurs as the components migrate up the TLC plate, the spots obtained after elution of the analyte mixture are less concentrated than when the analyte was originally spotted on the TLC plate. Therefore, the method of the present invention is not thin layer chromatography (TLC), and can best be described as the opposite of TLC or a non-TLC procedure. This distinction is discussed, for example, in pages 2 and 3 of the present patent application. In TLC, the components of the analytes separate, but with the present invention components of the analyte do not separate but are concentrated at a small spot where they are deposited on the plate by capillary action. Migration of the analyte on the TLC plate is contrary to optimization of the results of the present invention. As a result, better detection sensitivity is obtained from the present invention when compared to TLC and other spot test methods. TLC methods reported in the literature often cite lower levels of detection of analytes at the 100, 50, 10 and 1

microgram levels. In the present invention, detection of analytes at the 100 nanogram (0.1 microgram) and 10 nanogram levels occur, as discussed on page 30 of the specification. The specification sets forth that the test method of the present invention is generally solvent dependent, with respect to the solvents for the analyte and the detector reagent, and the polarity of the sorbent material.

As understood, Tyihak discloses a linear overpressurized thin-layer chromatographic apparatus where capillary tubes 6 and 7 are connected to a sorbent layer plate 1. The samples are fed into the apparatus containing the sorbent layer by overpressure applied to the capillary tube, column 4, lines 49-55. Further, the analyte does not appear to remain at the place of deposition, but migrates across the sorbent plate under pressure.

It is further believed that the invention disclosed in this application is sufficiently distinct from TLC, even though a common feature is the use of sorbent plates. Even waiving this argument still leaves a core result that the present invention is able to detect chromatographic sensitivities much greater than those obtained with conventional TLC methods. Further the microspot test and system of the present invention does not utilize an elution step, and the analyte compounds are not generally separated when the microspot test method is performed

For the reasons cited above, Tyihak does not appear to disclose, teach or show a sorbent material means having a detector reagent pre-deposited in the sorbent material and the sorbent material means adsorbing and concentrating the analyte at the spot of contact between the end portion of the tube means with the sorbent material means.

Further, Tyihak does not suggest that the analyte remains at the spot or place of contact between the end portion of the tube means with the sorbent material.

(2) Claim 14. Dependent claim 14 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening. Tyhak, as understood, does not appear to disclose or teach the limitation where the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening (see page 11, line 15 to page 12, line 2 of the specification).

(3) Claim 15. Dependent claim 15 recites a further feature of the system of claim 13 wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means. Tyhak, as understood, does not appear to disclose or teach the limitation where the thickness of the end wall is at least twice the diameter of the microcapillary sized opening, (see page 11, line 15 to page 12, line 2 of the specification)

b. Rejection of claims 17-27 for being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Tyihak (U.S. Patent No. 4,346,001). The claims of the group do

not stand and fall together and have been further grouped since they present different patentable features.

(1) Claim17. Dependant claim 17 recites a further feature of the system of claim 13 where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters. Tyhak, as understood, does not appear to either disclose or teach the limitation where the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters, (see page 9, lines 20 to 22 of the specification).

(2) Claim 18. Dependent claim 18 recites a further feature of the system of claim 13 where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters. Tiyhak, as understood, does not appear to either disclose or teach the limitation where the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters, (see page 9, line 18 to page 10, line 5 of the specification).

(3) Claim 19. Dependent claim 19 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer. As understood, Tihyak does not appear to suggest or teach a sorbent material comprising a thin layer chromatographic sheet provided with a silica gel surface layer.

(4) Claim 20. Dependent claim 20 recites a further feature of the system of claim 13 where the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent. As understood, Tihyak does not appear to suggest or teach a sorbent material comprising a thin layer chromatographic sheet provided with a polysilic acid sorbent.

(5) Claim 21. Dependent claim 21 recites a further feature of the system of claim 20 where the detector reagent is selected from the group consisting of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine. As understood, Tihyak does not appear to suggest or teach a detector reagent selected from the above identified group and pre-deposited in the sorbent material.

(6) Claim 22. Dependent claim 22 recites a further feature of the system of claim 13 where the the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material. As understood, Tihyak does not appear to suggest or teach a sorbent material formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

(7) Claim 23. Dependent claim 23 recites a further feature of the system of claim 13 where the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of sorbent materials and solvents.

(8) Claim 24. Dependent claim 24 recites a further feature of the system of claim 13 where the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected

from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of solvents and sorbent materials.

(9) Claim 25. Dependent claim 25 recites a further feature of the system of claim 13 where the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution with a pH in the range 2-12, dimethylsulfoxide, N-methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-

butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane. As understood, Tihyak does not appear to suggest or teach selected groups of solvents and sorbent materials.

(10) Claim 26. Dependent claim 26 recites a further feature of the method of claim 2 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination. **The rejection of this claim is not understood since it depends from an allowed claim 2, see copy of allowed claims in Appendix B.**

(11) Claim 27. Dependent claim 27 recites a further feature of the system of claim 13 where the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector

reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination. As understood, Tihyak does not appear to suggest or teach the selected sorbent materials.

It is requested that the rejections of all pending claims be reversed and all pending claims be allowed.

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9. **Appendix A: Appealed Claims**

Claims 13 through 27, as amended, are Appealed

13. (Twice Amended) A system for screening solutions containing an analyte and for detecting the presence of the analyte, comprising:

means for obtaining a solution containing the analyte;

tube means for receiving the solution containing the analyte, the tube means having an end portion with a microcapillary sized opening formed therein for dispensing the solution containing the analyte by capillary action;

sorbent material means having a detector reagent pre-deposited in the sorbent material for detecting the presence of the analyte, the sorbent material means receiving the solution containing the analyte from the tube means as the end portion of the tube means having the microcapillary sized opening is brought in contact with the sorbent material means so the solution containing the analyte is deposited on the sorbent material means by capillary action where the detector reagent has been pre-deposited and with the analyte being adsorbed by and concentrated in the sorbent material and remaining at the spot of contact between the end portion of the tube means with the sorbent material means for combining with the detector reagent.

14. The system according to claim 13, wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least equal to the diameter of the microcapillary sized opening.

15. (Once Amended) The system according to claim 13, wherein the microcapillary sized opening is defined by an end wall of the end portion of the tube means and the thickness of the end wall is at least twice the diameter of the microcapillary sized opening to reinforce the end portion of the tube means and to provide uniform sealing contact between the end wall and the sorbent material means when the tube means is placed in contact with the sorbent material means.

16. The system according to claim 13, wherein the tube means is selected from the group of microcapillary tubes, micropipets and micropipet tips.

17. The system according to claim 13, wherein the diameter of the microcapillary sized opening has range of between about 0.05 to about 1.6 millimeters.

18. The system according to claim 13, wherein the volume of a microcapillary tube or a micropipet is between about 0.1 to about 30 microliters.

19. (Once Amended) The system according to claim 13, wherein the sorbent material means comprises a thin layer chromatographic sheet provided with a silica gel surface layer.

20. (Once Amended) The system according to claim 13, wherein the sorbent material means comprises a thin layer chromatographic medium provided with a polysilicic acid sorbent.

21. The system according to claim 20, wherein the detector reagent is selected from the group consisting of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenyl acetate: sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M), ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodine plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

22. The system according to claim 13, wherein the sorbent material is formed of a polar silica gel material and the solvent for the solution containing the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

23. The system according to claim 13, wherein the sorbent material is a polar material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the

solvent for the analyte is a non-aqueous solvent that is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

24. The system according to claim 13, wherein the detector reagent comprises a solution in which the detector reagent is dissolved in a polar solvent and deposited on the sorbent material, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and wherein the solvent for the analyte is less polar than the sorbent material and is selected from the group comprising hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

25. The system according to claim 13, wherein the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, cellulose, polyamide, reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, silica gel modified with amino groups, silica gel modified with cyano groups, Kieselghur impregnated with hydrocarbons, anionic and cationic anion exchange resins, diethylaminoethyl cellulose, and mixtures of the listed sorbents, and the solvent for the analyte is selected from the group comprising acetic acid, water, aqueous buffer solution with a pH in the range 2-12, dimethylsulfoxide, N-

methylpyrrolidone, N,N-dimethyl acetamide, N,N-dimethyl formamide, propylene carbonate, acetonitrile, 2-methoxyethanol, diethylcarbonate, pyridine, methanol, acetone, ethanol, beta-phenethylamine, 2-ethoxyethanol, dioxane, methyl ethyl ketone, methyl n-propyl ketone, methyl acetate, methyl isobutyl ketone, chloroform, tetrahydrofuran, n-propanol, methyl isoamyl ketone, ethyl acetate, 2-methoxyethylacetate, isobutyl alcohol, n-butyl acetate, 2-butanol, 2-propanol, 1-butanol, ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

26. The method of claim 2, wherein the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

27. The system according to claim 13, wherein the sorbent material comprises a porous medium formed of two layers, the top layer formed of a sorbent substance and a detector reagent on or within a porous support, and wherein the analyte is deposited in the top

layer, and the bottom layer is formed a porous absorbent material containing a compound that dissolves in water to form a solution that wets the top layer, and the compound in aqueous solution reacts with the substance produced due to the reaction or interaction of the analyte with the detector reagent in the top layer, thereby producing a color change, or a change in fluorescence under ultraviolet illumination.

10. **Appendix B: All wed Claims**

Claims 1 through 11, as amended, have been **allowed.**

1.(Once Amended) A method of detecting the presence of an analyte, comprising the steps of:

placing a chromogenic or fluorogenic detector reagent for detecting the presence of the analyte on a chromatographic sheet or medium containing sorbent material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, aluminum oxide, and mixtures of therof;

placing the analyte in a solution where the solvent for the analyte consists of a non-aqueous solvent selected from the group of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane;

placing the solution containing the analyte in a tube having an end portion with a microcapillary sized opening, so that when the tube is placed in contact with a chromatographic sheet having a surface layer formed of sorbent material, the solution containing the analyte is withdrawn from the end portion of the tube and onto the surface layer of the sorbent material by capillary action;

placing the end portion of the tube having the microcapillary sized opening in contact with the sorbent material at the place where the detector reagent has been deposited on the sorbent material so that the solution containing the analyte is withdrawn from the tube by capillary action, the solvent being absorbed into the sorbent material and the analyte being separated from the solvent, and wherein the analyte remains at the spot of application and wherein the analyte is analyzed at this spot of application.

2. (Once Amended) A method of screening a solution for an analyte that has been dissolved in a solvent to form the solution and for detecting the presence of the analyte when the solution is deposited in a sorbent material so that the analyte is separated from the solvent at the place of application to the sorbent material, comprising the steps of:

placing a detector reagent for detecting the presence of the analyte on the sorbent material;

placing the solution containing the analyte in a tube having an end portion forming a microcapillary sized opening in the end portion of the tube so that when the tube is placed in contact with the sorbent material, the solution containing the analyte in the tube is withdrawn from the end portion of the tube and into the sorbent material by capillary action;

placing the end portion of the tube forming the microcapillary sized opening in contact with the sorbent material at the location where the detector reagent is placed on the sorbent material, so that the solution is withdrawn from the tube by capillary action, the solvent being absorbed into the sorbent material and the analyte being separated from the solvent and adsorbed by the sorbent material at the spot of application, wherein the analyte remains at the spot of application and is analyzed at this same spot.

3. The method of claim 2, wherein the diameter of the microcapillary sized opening has range of diameters of from about 0.05 to about 1.6 millimeters.

4. The method of claim 2, wherein the sorbent material is formed of a polar material selected from the group consisting of silica gel, high performance thin layer

chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and the solvent for the analyte is a non-aqueous solvent that is less polar than the sorbent material and selected from the group of ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

5. The method of claim 2, wherein the sorbent material comprises a thin layer chromatographic medium containing a silica gel or polysilicic acid sorbent and the solvent for the analyte is selected from the group consisting of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexane, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

6. The method of claim 2, wherein the detector reagent is selected from the group of bromcresol green; 7,7,8,8-tetracyanoquinodimethane (TCNQ); gold chloride; gold chloride/NaOH solution; 4-(4'-nitrobenzyl)pyridine/NaOH; cholinesterase/indoxyl acetate; cholinesterase/2,6-dichloroindophenylacetate, sodium pyrophosphate peroxide/aromatic amine; potassium bismuth iodide; 1 ,3-diisonitrosoacetone guanidinium salt; bis(diethylamino)benzophenone oxime; bis(diethylamino)benzophenone; bis(dimethylamino)thiobenzophenone; phenylazoformic acid 2-diphenylhydrazide; diphenylcarbazone; diphenylthiocarbazone; mercuric salt; diethyldithiocarbamic acid silver salt; 2, 2'-

dithiobis(5-nitropyridine); 5,5'-dithiobis(2-nitrobenzoic acid), Ellman's Reagent; molybdenum oxide in sulfuric acid; ammonium molybdate; iodine/starch; and sulfuric acid (4M); ammonium sulfate; ammonium cerium(IV)sulfate; ammonium iron(II)sulfate; cobalt(II)thiocyanate; palladium(II)chloride; potassium iodide plateate; sodium tetraphenyl boron; o-tolidine; and N,2,6-trichloro-p-benzoquinoneimine.

7. The method of claim 6, wherein the sorbent material is a polar material selected from the group of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide, and the solvent for the analyte is selected from solvents that are less polar than the sorbent material and selected from the group consisting of ethylene dichloride, dichloromethane, ethyl ether, o-dichlorobenzene, chlorobenzene, benzene, o-xylene, m-xylene, p-xylene, methyl tertiary-butyl ether, toluene, carbon tetrachloride, trichloroethylene, n-butyl chloride, hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

8. The method of claim 2, wherein the sorbent material is a chromatographic material selected from the group consisting of silica gel, high performance thin layer chromatography (HPTLC) silica gel, polysilicic acid, and aluminum oxide and mixtures thereof, and the solvent for the analyte is selected from the group consisting of hexadecane, nonane, cyclohexane, trimethylpentane, petroleum ether, iso-hexanes, hexane, heptane, cyclopentane, trichlorotrifluoroethane, and pentane.

9. The method of claim 2, wherein sorbent material is formed of a polar chromatographic material and the solvent for the analyte is a non-aqueous solvent that has a lower polarity than the sorbent material.

10. The method of claim 2, wherein the sorbent material is formed of a non-polar material selected from the group of reversed phase silica Gel C_2 (dimethyl bonded), reversed phase silica gel C_2 (ethyl bonded), reversed phase silica gel C_8 (octyl bonded), reversed phase silica gel C_{18} (octadecyl bonded), acetylated cellulose, and the solvent for the analyte is an aqueous solvent mixture containing solvents selected from the from the group of water, methanol, acetonitrile, and acetone.

11. The method of claim 2, wherein the sorbent material is formed of an ion-exchange material selected from the group of anion exchange resin, cation exchange resin and diethylaminoethylcellulose and the solvent for the analyte comprises water.